## Sources of Exposure

# Toxicokinetics and Biomonitoring

### Biomarkers/Environmental Levels

### **General Populations**

- There are no known natural sources of dinitrophenols.
- The general population can be exposed to low levels of dinitrophenols through ingestion of contaminated food and water and inhalation.
- In the 1930s, 2,4-dinitrophenol was used as a weight-reducing agent. This used was banned in 1938 due to severe health risks, including death. In recent years, however, 2,4-dinitrophenol, in tablet and powder form, has been illegally marketed for weight loss and body building by unregulated internet sources, leading to potential exposure.

# **Occupational Populations**

 Occupational exposure may occur for workers employed in the chemical manufacturing industry and munitions manufacturing industry.

### **Toxicokinetics**

- Information on absorption, distribution, and metabolism of dinitrophenols is limited to the 2,4-dinitrophenol isomer.
- 2,4-Dinitrophenol is absorbed by the oral, inhalation, and dermal routes.
- A portion of 2,4-dinitrophenol in the blood is bound to serum proteins, and the unbound fraction enters organs, including the eye.
- 2,4-Dinitrophenol is metabolized via sequential nitro group reduction to 2-amino-4-nitrophenol (predominant) and 4-amino-2-nitrophenol and then to 2,4-diaminophenol.
- 2,4-Dinitrophenol and its metabolites are excreted in the urine and, with profuse perspiration, can be excreted in sweat.

# **NHANES Biomonitoring**

No NHANES data available for dinitrophenols.

### **Biomarkers**

- 2,4-Dinitrophenol and its metabolites can be measured in blood and urine.
- Yellow staining of skin or sclera may indicate exposure to 2,4-dinitrophenol, although this is a nonspecific effect that can be caused by other chemicals or underlying health conditions.

### **Environmental Levels**

Air

There are no recent monitoring data for levels of dinitrophenols in air.

Water

- There are no recent monitoring data for levels of dinitrophenols in drinking water.
- Recent monitoring did not detect
   2,4-dinitrophenol in groundwater.
- At hazardous waste sites, the median 2,4-dinitrophenol level in water was 400 ppb.

Sediment and Soil

Recent monitoring did not detect 2,4-dinitropheno in soil or sediment. At hazardous waste sites, the median 2,4-dinitropheno level in water was 460,000 ppb.

### Reference

Agency for Toxic Substances and Disease Registry (ATSDR). 2021. Toxicological Profile for Dinitrophenols. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Services.

# ToxGuide<sup>TM</sup> for Dinitrophenols

 $C_6H_4N_2O_5$ 

(CAS # 51-28-5)
August 2021

U.S. Department of Health and Human Services Public Health Service Agency for Toxic Substances and Disease Registry www.atsdr.cdc.gov



# Chemical and Physical Information

## Routes of Exposure

## Relevance to Public Health (Health Effects)

# Dinitrophenols are Solids

- Dinitrophenols are a class of manufactured chemicals that do not occur naturally in the environment.
   There are six different isomers of dinitrophenol.
- Dinitrophenols are yellow crystalline solids that sublimate. They have no known odor.
- The most commercially important dinitrophenol is 2,4-dinitrophenol.
- Dinitrophenols can be explosive when dry.
- Dinitrophenols are used in the manufacturing of dyes, picric acid, picramic acid, wood preservatives, explosives, pH indicators, and photographic developers.

 Inhalation – Likely route of exposure for the general population and occupational population by inhaling contaminated air.

- Oral Most likely route of exposure for the general population through ingestion of contaminated food (including dietary supplements) and water.
- Dermal Not likely an exposure route of concern for the general population.

# Dinitrophenols in the Environment

- Environmental fate and transport of the different dinitrophenol isomers are likely to be similar.
- Dinitrophenols exist in both the vapor and particulate phase in the atmosphere, which influences their transport and removal. Dinitrophenols have been detected in rain, snow, and fog.
- The sorption and transport of dinitrophenols from water to suspended solids and sediment is greater in waters that are acidic and/or have high organic matter and clay content.
- Volatilization of dinitrophenols from water and soil is not likely to occur.
- Leaching of dinitrophenols from soil to groundwater decreases with increased organic carbon, clay, or goethite content in the soil and increased acidity of soil-
- Bioconcentration is not expected to be significant for dinitrophenols in aquatic organisms.

Health effects are determined by the dose (how much), the duration (how long), and the route of exposure.

### Minimal Risk Levels (MRLs)

Inhalation

 No acute-, intermediate-, or chronicduration inhalation MRLs were derived for dinitrophenols.

#### Oral

- No acute-duration oral MRL was derived for dinitrophenols.
- An intermediate-duration (15–364 days) oral MRL of 0.00007 mg/kg/day was derived for 2,4-dinitrophenol.
- No chronic-duration oral MRL was derived for dinitrophenols. The intermediate-duration oral MRL is expected to be protective for chronicduration oral exposures

### **Health Effects**

Information on health effects of dinitrophenols is limited to the 2,4-dinitrophenol isomer.

Oral and inhalation exposure to 2,4-dinitrophenol results in increased body temperature and basal metabolic rate, which elicit secondary effects.

- Secondary effects include decreased body weight or decreased weight gain; increased pulse, heart, and respiratory rate; nausea and vomiting; confusion, dizziness, and delirium; muscle pain and weakness; acute renal failure; and sometimes death.
- 2,4-Dinitrophenol exposure may also result in peripheral neuritis, agranulocytosis, erythematous and pruritic rashes with maculopapular eruptions, and cataracts.
- In animal studies, exposure to 2,4-dinitrophenol resulted in increased number of resorptions, stillborn pups, neonatal pup death, and decreased fetal/pup body weight and length.
- The Department of Health and Human Services, U.S. Environmental Protection Agency (EPA), and International Agency for Research on Cancer (IARC) have not evaluated the potential carcinogenicity of any of the dinitrophenol isomers.

### Children's Health

It is not known if children are more sensitive to dinitrophenol exposure than adults. However, studies in animals indicate that infants and children may be more sensitive.